

# Adaptive Resolution Simulation of Liquid Water

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We present a multiscale simulation of liquid water where a spatially adaptive molecular resolution procedure allows for changing on-the-fly from a coarse-grained to an all-atom representation. We show that this approach leads to the correct description of all essential thermodynamic and structural properties of liquid water.

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Scientific problems in physics are usually classified by typical scales of measurable quantities such as energy, length or time. The appropriately determined scale together with a tailored model and/or experiment is at the outset of a successful study. The specific properties under investigation then typically define the appropriate level of resolution. Using the optimal set of degrees of freedom (DOFs) guarantees efficiency, accuracy and avoids huge amounts of unnecessary detail, which might even obscure the underlying physics. This approach dates back to the very beginning of modern physics and finds its logical continuation in systematic coarse-graining efforts for modern computational materials science and biophysics problems [1, 2, 3, 4], where full blown all-atom simulations are often beyond the possibilities of current and near future computers. However, in many problems of materials science and biology different time- and length-scales are intrinsically interconnected, far beyond giving constant prefactors on the next coarser level of detail. Multiscale simulations are emerging as a promising tool for such problems [5, 6, 7, 8, 9]. Ideally, in addition to coarse-graining, one would like to make the step back to characteristic fine grained configurations as well [10, 11]. Recently, an adaptive multiscale scheme (AdResS) has been proposed by some of us that also allows a free exchange of particles between regions of different resolutions and to adjust locally the level of detail at will, while maintaining equilibrium with the fluctuating environment [12].

In this letter we address the above issue for liquid water, which continues to be a very active research field for the obvious reason, that all life exists in a water environment. Although many classical models have been developed for the simulation of liquid water [13, 14, 15, 16], there is still no unique model that can reproduce all its anomalous properties. Water is intrinsically multiscale, as it plays different roles at different scales. For instance, in the case of biomolecules in solution, at short length scales the hydrogen bonding with water governs the local shape and stability of folded biopolymers, whereas the “hydrophobic effect” drives the organization of the

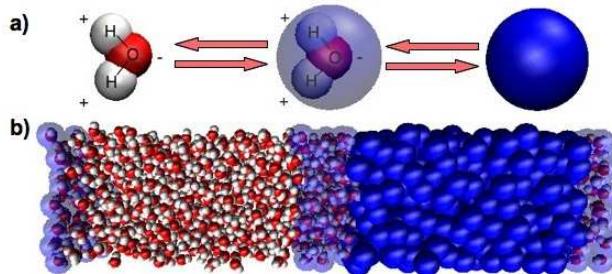


FIG. 1: (Color) On-the-fly interchange between the all-atom and coarse-grained water models. a) The explicit all-atom water molecule is represented at the left, and the coarse-grained molecule at the right. The middle hybrid molecule interpolates between the two, cf. text. A schematic representation of the full system is shown in b), where a hybrid region connects the explicit and coarse-grained levels of description. All the results presented in the paper were obtained by performing NVT simulations using ESPResSo [19] with a Langevin thermostat, with a friction constant  $\Gamma = 5ps^{-1}$  and a time step of  $0.002ps$  at  $T_{ref} = 300K$  and  $\rho = 0.96g/cm^3$  (the density was obtained from an NPT simulation with  $P_{ref} = 1 atm$ ). Periodic boundary conditions were applied in all directions. The box size is  $94.5 \text{ \AA}$  in the x and  $22 \text{ \AA}$  in the y and z direction. The width of the interface layer is  $18.9 \text{ \AA}$  in the x direction.

system at longer time and length scales (as for instance the formation of membranes in aqueous solution). The approach presented in this letter represent a first step towards multiscale modeling of such complex scenarios. For fluctuating systems, such as adsorption of water on a hydrophilic surface, we envision a system in which an atomistic description is needed only near the surface, and a mesoscopic resolution can be used for water molecules further away from it, with molecules freely moving around without “feeling” the local level of resolution.

To accomplish this goal, we first propose a new single-site water model that reproduces remarkably well the essential thermodynamic and structural features of water, as obtained by detailed all-atom simulations. In the second step we adapt the AdResS scheme to define a robust and physically accurate procedure to smoothly join the explicit atomistic and coarse-grained resolution regions. The resulting multiscale hybrid/mesoscopic model system [12, 17, 18] is composed of explicit and coarse-grained

molecules as presented in Figure 1.

**Coarse-graining of water** – Recent work has focused on simplified coarse-grained models that can reproduce qualitatively the all-atom center-of-mass (cm) radial distribution function (rdf) of water [20, 21, 22, 23, 24]. To reproduce further structural properties, such as the orientational preferences for nearest neighbor configurations (i.e. for hydrogen bonding), previous one-site models [21, 22] require a posteriori adjustment of the local environment [22]. The one-site model of water presented in this letter can reproduce the structural and thermodynamic properties of a widely used all-atom water model (namely, Rigid TIP3P [13]) with remarkable accuracy, without requiring any orientational corrections [25]. To construct the model we follow an iterative inverse statistical mechanics approach proposed by Lyubarstev *et al.* [26] (for alternative procedures see also Refs. [2] and [27]). The aim of this scheme is to numerically build a coarse-grained effective Hamiltonian that can mimic the behavior of a set of physical observables of the system under consideration (see i.e. Matysiak *et al.* [28, 29] where this idea has been used to define a coarse-grained protein Hamiltonian "anchored" to experimental data). Additionally, in order to match the pressure of the coarse-grained to the all-atom model, after each iteration, a weak constant force is added to the effective force in such a way that the total effective force and potential energy are zero at the 7 Å cutoff distance [17, 27].

Figure 2 shows the final results obtained when this procedure is applied to a box of water molecules. A perfect agreement between the all-atom and coarse-grained center-of-mass rdf's is reached with our optimized effective potential (shown in the inset of the figure) after 8 iterations. The effective potential has a first primary minimum at about 2.8 Å corresponding to the first peak in the center-of-mass rdf. The slightly weaker and significantly broader minimum at 4.5 Å corresponds to the second hydration shell. The combined effect of the two minima leads to a local packing close to that of the all-atom TIP3P water. Our effective coarse-grained potential is quite different from the previously suggested potentials [20, 21, 22]: while in previous one-site models the deepest minimum corresponds to the second hydration shell, the absolute minimum in our model is found in the first shell. In order to more thoroughly quantify the structural properties of our model (that are not completely defined by the rdf) we computed the angular distribution between the center-of-mass of three nearest neighbor molecules, and the distribution of the orientational order parameter  $q$  as defined by Errington *et al.* [30]:  $q = 1 - \frac{3}{8} \sum_{j=1}^3 \sum_{k=j+1}^4 \left( \cos \psi_{jk} + \frac{1}{3} \right)^2$ , where  $\psi_{jk}$  is the angle formed by the lines joining the oxygen atom of a given molecule and those of its nearest neighbors  $j$  and  $k$ . The parameter  $q$  measures the extent to which a molecule and its four nearest neighbors

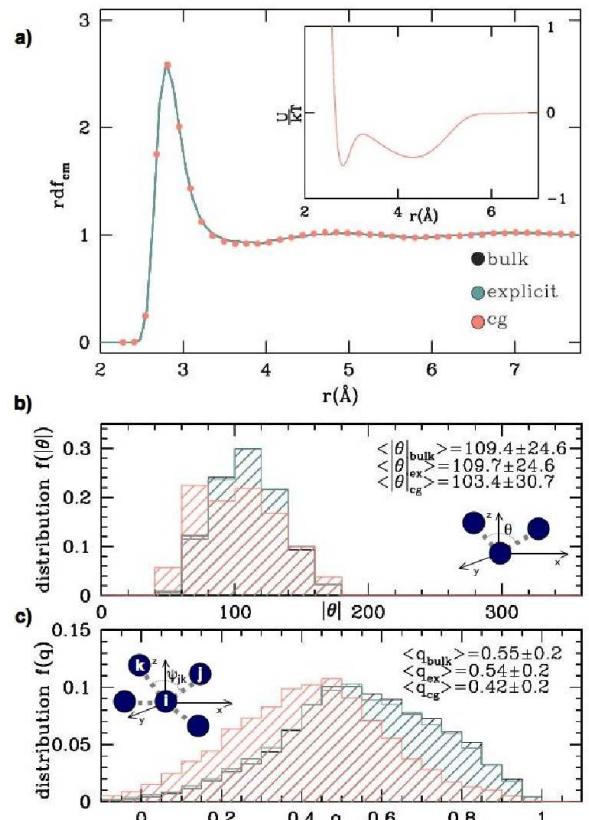


FIG. 2: (Color) a) The center-of-mass rdf's for explicit (ex) [cyan line] and coarse-grained (cg) [red line] regions of the hybrid system, are shown together with the rdf's corresponding to a bulk all-atom simulation (black line). The local O-H and H-H rdf's for the explicit molecules in the hybrid system compare equally well to the standard bulk simulations (not shown). The optimized effective potential for the coarse-grained model is shown in the inset as a function of inter-particle separation,  $r$ . (b) The center-of-mass angular distribution between three nearest neighbors for the three cases studied as given in (a). (c) The analogous distributions of the orientational order parameter  $q$ .

adopt a tetrahedral arrangement [30]. The good agreement between the explicit and coarse-grained water models shown in Figures 2 (b) and (c) indicates that although our coarse-grained model is spherically symmetric and therefore does not have any explicit directionality, it effectively captures the orientational preferences of hydrogen bonding.

As a consequence of the reduced number of DOFs, there is a time scale difference in the dynamics of the coarse-grained system, that is faster than what is predicted from all-atom simulations. The diffusion coefficient of the center-of-mass for the Rigid TIP3P model is  $D \approx (3.7 \pm 0.3) \times 10^{-9} \frac{m^2}{s}$  while for the coarse-grained model is  $D \approx (8.1 \pm 0.4) \times 10^{-9} \frac{m^2}{s}$ . While an accelerated time scale can be very advantageous in some cases, one can also adjust  $D$  by an increased background friction in the Langevin thermostat [2, 31].

**Multiscale procedure** – In order to smoothly join the atomistic and coarse-grained resolutions, we apply the AdResS scheme of Praprotnik *et al.* [12, 17] to couple a model system composed of explicit and coarse-

grained molecules. Half of the simulation box is occupied by atomistic (Rigid TIP3P) water molecules while the other half is filled with the same number of corresponding coarse-grained molecules as schematically presented in Figure 1. The two regions freely exchange molecules through a transition regime, where the molecules change their resolution and their number of DOFs accordingly. The interface region contains hybrid molecules that are composed of an all-atom molecule with an additional massless center-of-mass particle serving as an interaction site. The transition, which needs to be smooth in order to be used in MD simulations, is governed by a weighting function  $w(x) \in [0, 1]$  that interpolates the interaction forces between the two regimes, and assigns the identity of the particle. We used the weighting function defined in [12], in such a way that  $w = 1$  corresponds to the atomistic region, and  $w = 0$  to the coarse-grained region, whereas the values  $0 < w < 1$  correspond to the interface layer. The atomic and mesoscopic length scales are coupled via the intermolecular force acting between centers of mass of molecule  $\alpha$  and  $\beta$  as:

$$\mathbf{F}_{\alpha\beta} = w(X_\alpha)w(X_\beta)\mathbf{F}_{\alpha\beta}^{atom} + [1-w(X_\alpha)w(X_\beta)]\mathbf{F}_{\alpha\beta}^{cm}, \quad (1)$$

where  $\mathbf{F}_{\alpha\beta}^{atom} = \sum_{i_\alpha, j_\beta} \mathbf{F}_{i_\alpha j_\beta}^{atom} = -\sum_{i_\alpha, j_\beta} \frac{\partial U^{atom}}{\partial \mathbf{r}_{i_\alpha j_\beta}}$  is the sum of all pair intermolecular atom interactions between explicit atoms of the molecules  $\alpha$  and  $\beta$  and  $\mathbf{F}_{\alpha\beta}^{cm} = -\frac{\partial U^{cm}}{\partial \mathbf{R}_{\alpha\beta}}$  is the corresponding effective intermolecular force between their centers of mass.  $\mathbf{r}_{i_\alpha j_\beta} = \mathbf{r}_{i_\alpha} - \mathbf{r}_{j_\beta}$  is the vector between atom  $i$  in molecule  $\alpha$  and atom  $j$  in molecule  $\beta$  and  $\mathbf{R}_{\alpha\beta} = \mathbf{R}_\alpha - \mathbf{R}_\beta$  the vector between the centers of mass of molecules  $\alpha$  and  $\beta$ , with the corresponding  $X$  coordinates  $X_\alpha$  and  $X_\beta$ . Each time a molecule crosses a boundary between the different regimes it gains or loses (depending on whether it leaves or enters the coarse-grained region) its equilibrated rotational DOFs while retaining its linear momentum. To supply or remove the latent heat caused by the switch of resolution this method is employed together with a Langevin thermostat [12]. As discussed in an earlier publication, it is important to interpolate the forces and not the interaction potential if the Newton's Third Law is to be satisfied [18]. The key methodological issue in applying our approach to water is how to treat the long-range electrostatic interactions. We have chosen the reaction field (RF) method, in which all molecules with the charge center outside a spherical cavity of a molecular based cutoff radius  $R_c = 9\text{\AA}$  are treated as a dielectric continuum with a dielectric constant  $\epsilon_{RF}$  [32, 33, 34, 35]. The Coulomb force acting on a charge  $e_{i_\alpha}$ , at the center of the cutoff sphere, due to a charge  $e_{j_\beta}$  within the cavity is:

$$\mathbf{F}_{C_{i_\alpha j_\beta}}^{atom}(\mathbf{r}_{i_\alpha j_\beta}) = \frac{e_{i_\alpha} e_{j_\beta}}{4\pi\epsilon_0} \left[ \frac{1}{r_{i_\alpha j_\beta}^3} - \frac{1}{R_c^3} \frac{2(\epsilon_{RF} - 1)}{1 + 2\epsilon_{RF}} \right] \mathbf{r}_{i_\alpha j_\beta}. \quad (2)$$

There are three main reasons that make the RF method a natural choice to be applied with our scheme (Eq. 1): the first reason is that it does not impose any artificial periodicity (that would interfere with the definition of the interface layer of the system), the second one is the pairwise form of the reaction field term (Eq. 2), and the third one is that, as our scheme, the RF method works accurately only in a combination with a thermostat [34]. The last point can be better understood if the switching of the resolution is seen as a geometry induced phase transition [18]. Detailed comparisons between the bulk explicit simulations and the explicit regime in our hybrid setup prove that this approach does not alter the structural properties of the water model studied. The width of the interface layer is determined by the maximum range of electrostatic interactions, in order to allow the molecules to equilibrate on-the-fly while moving from one resolution to the other. In order to obtain a very smooth density distribution in the interface layer we use a conservative choice, that is, double the maximum range of interactions; however, a smaller interface layer can be used without affecting the fluxes between the layers, nor the results in the two resolution regimes. We observed that for a system containing only hybrid molecules, the pressure is increased in comparison to the reference all-atom system with the maximum deviation at  $w = 1/2$  (280% difference). This problem is solved by employing an interface pressure correction [17].

The structural (see Figure 2) and thermodynamic properties of the bulk all-atom simulations are correctly reproduced in the hybrid system with the same mean temperature (0.1% difference) and pressure (0.5% difference). The normalized density for the hybrid system is homogeneous in the coarse-grained and explicit regions with (very) small oscillations in the transition regime, cf. Figure 3. In order to prove the free exchange of molecules between the different regimes we have computed the time evolution of a diffusion profile for molecules that were initially localized at the interface layer. Figure 3 shows that these molecules spread out asymmetrically with time. This asymmetry arises from the aforementioned difference in diffusion coefficient between the all-atom and coarse-grained regions. It is possible to obtain the same diffusional dynamics across the different resolutions by adding a local Langevin thermostat, as mentioned above [36]. However, it is worth noticing that this difference in time scale can be advantageous for reaching longer simulation times in systems where multiple length and time scales are intrinsically present.

In this letter a general and computationally efficient multiscale model for water has been presented. We have shown that a one-site coarse-grained model for water molecules can reproduce remarkably well thermodynamic and structural properties of the Rigid TIP3P water model, and that a smooth transition and free exchange between coarse-grained and all-atom resolutions

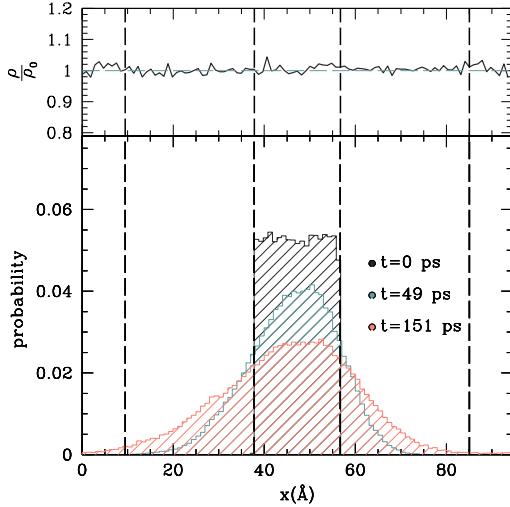


FIG. 3: (Color) Top figure: normalized density profile in the  $x$ -direction of the hybrid system. Bottom figure: Time evolution of a diffusion profile for the molecules that are initially (at time  $t = 0$  ps) located in the interface region. The diffusion profile is averaged over  $\approx 400$  different time origins. Vertical lines denote the boundaries of the interface layer.

is possible. We stress that the presented multiscale approach can be applied to any other either flexible or rigid nonpolarizable classical water model, e.g. SPC or SPC/E [35, 37, 38]. We envision that such a multiscale resolution of water will play an important role in the modeling of wet/dry interfaces and biomolecular simulations.

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